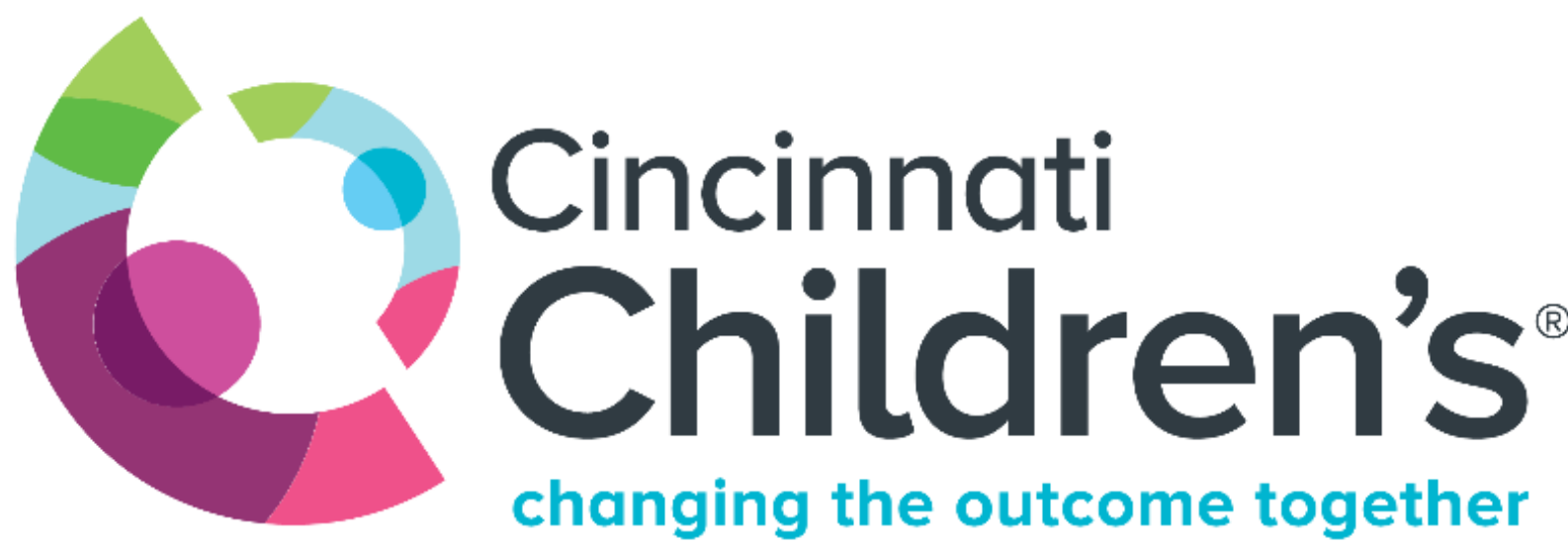


Vitamin D Deficiency Is Prevalent And Resistant To Correction In Patients With Hemophagocytic Lymphohistiocytosis (HLH)

Jennifer Jess, MD; Bethany Verkamp, MD; Allison Bartlett, MD; Michael Jordan, MD



Background

- Vitamin D plays a key role in immunoregulatory functions.
- Hematopoietic cell transplant (HCT) can lead to worsening nutrient deficiencies due to increased nutritional requirements, inflammation, mucosal barrier breakdown and infection.
- Vitamin D deficiency at the time of HCT is associated with worse outcomes.
- Standard repletion often does not sufficiently replete Vitamin D levels in patients undergoing HCT leading to use of very high dose-replacement regimens, called ‘Stoss’ dosing (one time dose of 7000-14000 U/kg)

Objectives

- Characterize the incidence and impact of Vitamin D insufficiency in patients with hemophagocytic lymphohistiocytosis (HLH) undergoing HCT.
- Investigate the use of standard repletion versus high-dose Stoss therapy on the ability to achieve sufficient levels pre-HCT.

Methods

- Retrospective chart review was performed on 137 patients with HLH undergoing their first HCT at Cincinnati Children’s Hospital Medical Center from 2010 to 2023.
- Demographic data, vitamin D levels at pre-determined time points, vitamin D supplementation received (Stoss and/or standard therapy), length of supplementation, length of steroid exposure, and post-transplant outcomes were recorded.

Results

Name	Vitamin D Deficient n=76	Vitamin D Sufficient n=8
Gender, n (%)		
Male	44 (58)	5 (62)
Female	32 (42)	3 (38)
Age at HCT, months median (range)	25.5 (3-305)	8 (2-71)
Race, n (%)		
African American	10 (13)	0 (0)
Chinese	7 (9)	0 (0)
Caucasian	57 (75)	8 (100)
Native Hawaiian	2 (3)	0 (0)
Diagnosis, n (%)		
Primary HLH	65 (85)	8 (100)
EBV driven HLH	9 (12)	0 (0)
VUS/other	2 (3)	0 (0)

Table 1: Demographic Data and Patient Characteristics. Primary HLH includes patients with a genetically validated diagnosis and/or known family history of HLH. *HLH* - hemophagocytic lymphohistiocytosis; *EBV* - Epstein-Barr Virus; *VUS* – variant of unclear significance

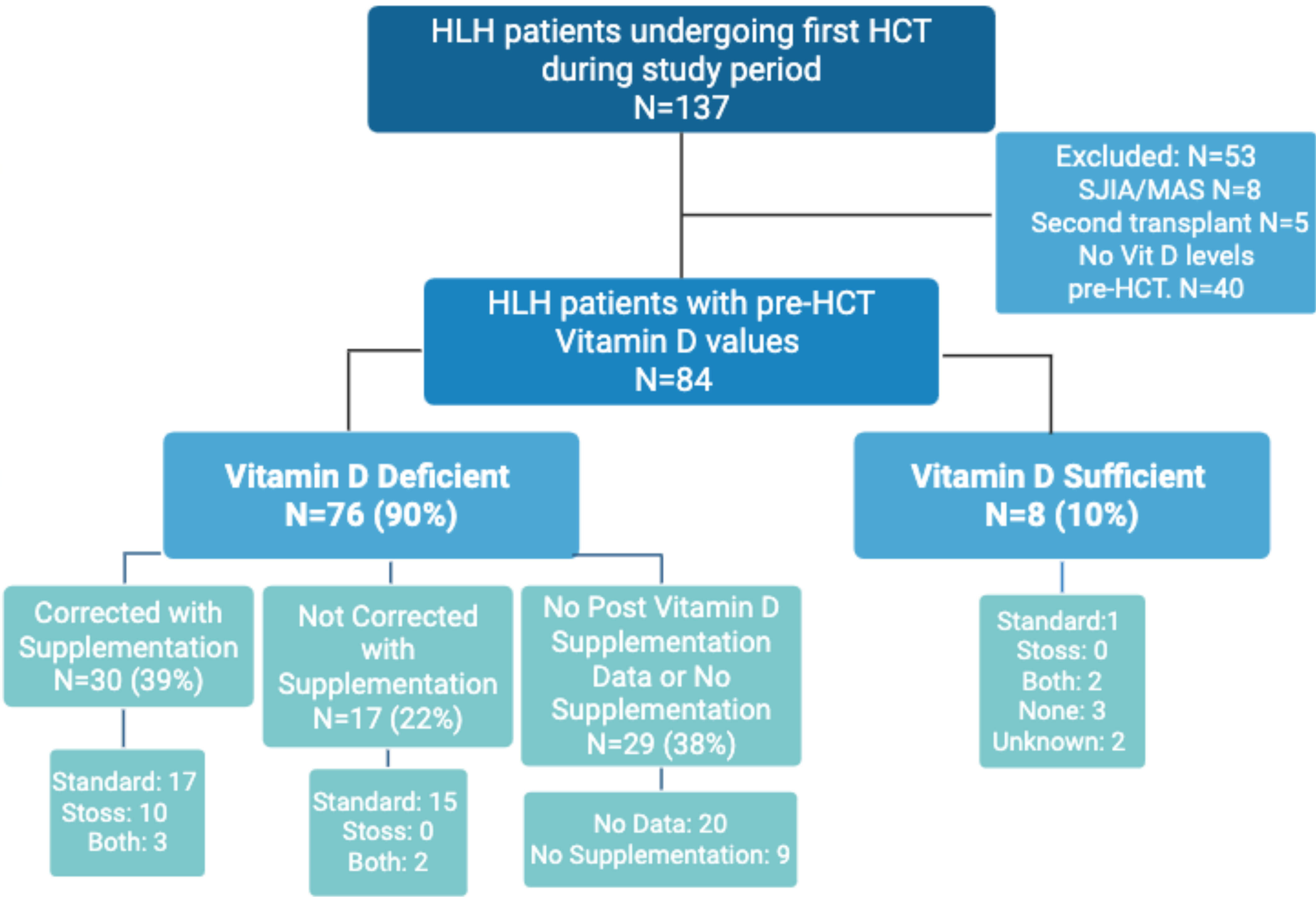


Figure 1: Prevalence of Vitamin D Deficiency in Patients with HLH at time of Hematopoietic stem cell transplantation (HCT). SJIA - systemic juvenile idiopathic arthritis; MAS - macrophage activation syndrome.

Conclusions

- Patients with HLH have a very high incidence of vitamin D deficiency (90%) prior to HCT.
- These rates appear to be higher than the 70% that has been reported in the general pediatric HCT population.
- Patients often require aggressive repletion to achieve sufficient levels, using standard supplementation and/or Stoss therapy.

Future Directions

- Examine the impact of steroid exposure on vitamin D levels
- Describe optimal timing and degree of Vitamin D supplementation needed to achieve and maintain sufficiency.
- Correlate vitamin D levels pre-HCT with outcomes post-HCT, including incidence of TMA, mixed chimerism, and mortality.
- Examine additional fat-soluble vitamins, such as vitamin A, to determine if similar trends persist.

References

1.Mona Benrashid, Kim Moyers, Mohamad Mohty, Bipin N. Savani. Vitamin D deficiency, autoimmunity, and graft-versus-host-disease risk: Implication for preventive therapy, *Experimental Hematology*, Volume 40, Issue 4, 2012, Pages 263-267, ISSN 0301-472X, <https://doi.org/10.1016/j.exphem.2012.01.006> (<https://www.sciencedirect.com/science/article/pii/S0301472X12000082>)

2.Wallace G, Jodele S, Myers KC, et al. Single Ultra-High-Dose Cholecalciferol to Prevent Vitamin D Deficiency in Pediatric Hematopoietic Stem Cell Transplantation. *Biol Blood Marrow Transplant*. 2018;24(9):1856-1860. doi:10.1016/j.bbmt.2018.05.019

3. Wallace G, Jodele S, Howell J, et al. Vitamin D Deficiency and Survival in Children after Hematopoietic Stem Cell Transplant. *Biol Blood Marrow Transplant*. 2015;21(9):1627-1631. doi:10.1016/j.bbmt.2015.06.009

4. Images: Created in <https://BioRender.com>